REMARKS

Claims 121-132, 140 and 141 are pending in the subject application. By this Amendment, applicants have amended claims 121 and 140. Accordingly, claims 121-132, 140 and 141 will be pending in the subject application upon entry of this Preliminary Amendment.

In view of the arguments below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Sequence Requirements

The Examiner stated that the application fails to comply with the requirements of 37 C.F.R. §§1.821-1.825. Specifically, the Examiner states that the disclosure contains sequences that need SEQ ID numbers on page 11, lines 28-31, of the instant specification.

In response, applicants note that the specification has been amended to reflect the proper SEQ ID numbers. Accordingly, applicants maintain that the application complies with the requirements of 37 C.F.R. §§1.821-1.825.

Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 121-132, 140 and 141 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains,

or with which it is most nearly connected, to make and/or use the invention.

In response, applicants respectfully traverse the Examiner's rejection.

The test for enablement is whether one skilled in the art could, at the time of the invention, make and use the claimed invention based on the disclosure and the information known in the art without undue experimentation. Applicants maintain that the claimed invention satisfies the test for enablement, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

The subject invention comprises a method for identifying compounds that inhibit the binding of a CD4 receptor, a p75 receptor, a serotonin 2A receptor, a serotonin 2B receptor, a NMDA receptor, a K^+ channel, or a composition comprising a peptide selected from the group consisting of amino acid sequences as set forth in SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16 with a cytoplasmic protein containing the amino acid sequence (G/S/A/E)-L-G-(F/I/L). This invention is based, in relevant part, on applicants' discovery of the new consensus sequence (S/T)-X-(V/I/L) composed of only three amino acids found in the carboxyl-terminus of signal transducing proteins that bind to PDZ domains of cytoplasmic proteins. Accordingly, the invention may be practiced using a CD4 receptor, a p75 receptor, a serotonin 2A receptor, a serotonin 2B receptor, a NMDA receptor, a K^+ channel, or a composition comprising a peptide selected from the group consisting of

amino acid sequences as set forth in SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16, all of which contain a sequence within the consensus sequence, to find compounds that will alter the binding of the carboxyl terminus domain to the PDZ domain of cytoplasmic proteins.

In support of the rejection, the Examiner alleges that the specification does not reasonably enable the claimed methods because it allegedly calls for the use of trial and error to attempt to find a compound that will inhibit the specific interaction between a signal transducing protein and a cytoplasmic protein. Therefore, the Examiner concludes that given the breadth of the claims with respect to the scope of the disclosure of the specification and what is known in the prior art, one skilled in the art would be forced to engage in undue experimentation in order to make or use the subject invention.

Applicants strongly disagree with the Examiner's position.

According to M.P.E.P. § 2164.05(a), "[t]he state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling". *In re Gunn*, 537 F.2d 1123, 1128, 190 USPQ 402, 405 (CCPA 1976). However, the specification "need not disclose what is well-known to those skilled in the art". *In re* Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Applicants maintain that the disclosure provides guidance including a working example which, when combined with the knowledge of the prior art, is sufficient to enable one skilled in the art to

practice the instant method. As the Examiner concedes, the disclosure describes an assay for identifying potential compounds that inhibit Fas/FAP1 binding. The Examiner further alleges that no compound that works has been found.

In response, applicants point the Examiner's attention to the instant specification, *inter alia* at page 24, line 5, to page 25, line 25, where a method for screening for candidate compounds and the synthesis of those compounds is disclosed. Applicants further point the Examiner's attention to the instant specification, *inter alia* at page 27, lines 8-10, where compounds such as Ac-SLV and Ac-SLY, which were successfully used to inhibit the interaction between Fas and FAP1, are disclosed. Therefore, applicants maintain that the disclosure provides compounds which inhibit the specific binding between a signal transducing protein and a cytoplasmic protein in addition to a working example detailing the screening of potential compounds to be used in the claimed methods. Further, applicants note that the screening method given as an example was well-known to one skilled in the art at the time of the filing of this application. Given the details of the consensus sequence and of the interaction between a signal transducing protein and a cytoplasmic protein found in the disclosure, one skilled in the art would easily recognize the necessary steps to narrow down the group of compounds to be used in the claimed methods as potential inhibitors of the interaction between a CD4 receptor, a p75 receptor, a serotonin 2A receptor, a serotonin 2B receptor, a NMDA receptor, a K^+ channel, or a composition comprising a peptide selected from the group consisting of amino acid sequences as set forth in SEQ ID NO:9, SEQ ID NO:11, SEQ ID

NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16 and a cytoplasmic protein containing the amino acid sequence (G/S/A/E)-L-G-(F/I/L).

Accordingly, applicants maintain that the direction and detailed working example disclosed in the subject specification in combination with the state of the prior art and the level of one of ordinary skill at the time of filing satisfy the requirements for enablement of 35 U.S.C. §112, first paragraph.

The Examiner further rejected claims 121-132, and 139-141 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that applicants had possession of the invention.

Specifically, the Examiner alleges that the claims contain new subject matter. The Examiner alleges that amended claim 121 *adds* the limitation that the compound forms a complex with the signal transducing protein. The Examiner further alleges that the limitation to the signal transducing protein being "a composition comprising a peptide selected from the group consisting of amino acid sequences as set forth in SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16" is not supported by the disclosure.

In response, applicants respectfully traverse the Examiner's rejection.

Applicants maintain that the amendments to claim 121 did not *add* the limitation that the compound forms a complex with the signal transducing protein. Applicants direct the Examiner's attention to page 65, line 28, of the instant specification, where original claim 27, which corresponds to claim 121, was filed reciting the limitation "to form a complex". In addition, applicants direct the Examiner's attention to page 6, lines 9-28, page 11, lines 26-31, and Figure 2, where SEQ ID NOs. 9 and 11-16 are disclosed, specifically as interacting with the PDZ domain of FAP1. Accordingly, applicants maintain that claim 121 as amended does not include new matter.

The Examiner further rejected claims 121-132, 140 and 141 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner alleges that the applicant was not in possession of the claimed genus of proteins. Specifically, the Examiner states that in the absence of structural characteristics that are shared by members of the genus of "CD4 receptors, p75 receptors, serotonin 2A receptors, NMDA receptors, K channels, or any peptide comprising SEQ ID NO:9, SEQ ID NOs. 11-16, or cytoplasmic proteins or compounds" identified by the claimed method, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus.

In response, applicants respectfully traverse the Examiner's rejection.

As stated above, and contrary to the Examiner's assertion, applicants note that the claimed invention comprises a *method*

for identifying compounds that inhibit the binding of a CD4 receptor, a p75 receptor, a serotonin 2A receptor, a serotonin 2B receptor, a NMDA receptor, a K^+ channel, or a composition comprising a peptide selected from the group consisting of amino acid sequences as set forth in SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16 with a cytoplasmic protein containing the amino acid sequence (G/S/A/E)-L-G-(F/I/L). A genus of compounds as envisaged by the Examiner is not the subject of claim 121. Nevertheless, applicants maintain that each group of proteins which form part of the method steps of claim 121 are clearly defined by identifying characteristics such as nucleic acid sequence and binding affinity and specificity. Specifically, the signal transducing proteins are described as comprising the consensus sequence(S/T)-X-(V/I/L) found at the carboxyl-terminus. The cytoplasmic proteins are described as comprising the amino acid sequence (G/S/A/E)-L-G-(F/I/L). In addition, the interaction between these two classes of proteins is disclosed. Applicants direct the Examiner's attention to the subject specification *inter alia* at page 3, lines 16-24, where a table lists representative examples of proteins that interact with PDZ domains and their associated cytoplasmic proteins. Accordingly, applicants maintain that the disclosure provides a sufficient description of the components of the claimed methods.

In view of these remarks, applicants maintain that claims 121-132, 140 and 141 satisfy the requirements of 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 121-132, 140 and 141 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Specifically, the Examiner states that claim 121 is indefinite for reciting "the cytoplasmic protein is no longer bound; and is no longer bound", "and the signal transducing protein bound to the cytoplasmic protein", "a method of identifying a compound" and "a known compound", and claim 140 is indefinite for reciting an explanation of symbols.

In response, but without conceding the correctness of the Examiner's rejection, applicants note that claims 121 and 140 have been amended to more clearly define the claimed methods, thereby obviating the rejection.

In view of these remarks, applicants maintain that claims 121-132, 140 and 141 satisfy the requirements of 35 U.S.C. §112, second paragraph.

Conclusion

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the rejections, and solicit allowance of the pending claims.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants'

undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with this Preliminary Amendment. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicants
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Commissioner for Patents,
P.O. Box 1450
Alexandria, VA 22313-1450

6/4/04

Alan J. Morrison Date
Reg. No. 37,399